H19 gene

H19, imprinted maternally expressed transcript (non-protein coding)

Normal Function

The *H19* gene provides instructions for making a molecule called a noncoding RNA. (RNA is a chemical cousin of DNA.) Unlike many genes, the *H19* gene does not contain instructions for making a protein. The function of the gene is unknown, but researchers believe that it may act as a tumor suppressor, keeping cells from growing and dividing too fast or in an uncontrolled way. This gene is highly active in various tissues before birth and appears to play an important role in early development.

People inherit one copy of most genes from their mother and one copy from their father. Both copies are typically active, or "turned on," in cells. However, the activity of the *H19* gene depends on which parent it was inherited from. Only the copy inherited from a person's mother (the maternally inherited copy) is active; the copy inherited from the father (the paternally inherited copy) is not active. This sort of parent-specific difference in gene activation is caused by a phenomenon called genomic imprinting.

H19 is part of a cluster of genes on the short (p) arm of chromosome 11 that undergo genomic imprinting. Another gene in this cluster, *IGF2*, is also involved in growth and development. A nearby region of DNA known as imprinting center 1 (IC1) or the H19 differentially methylated region (H19 DMR) controls the parent-specific genomic imprinting of both the *H19* and *IGF2* genes. The IC1 region undergoes a process called methylation, which is a chemical reaction that attaches small molecules called methyl groups to certain segments of DNA. Methylation, which occurs during the formation of an egg or sperm cell, is a way of marking or "stamping" the parent of origin. The IC1 region is normally methylated only on the paternally inherited copy of chromosome 11.

Health Conditions Related to Genetic Changes

Beckwith-Wiedemann syndrome

Beckwith-Wiedemann syndrome, a condition characterized by overgrowth and other signs and symptoms that affect many parts of the body, can result from changes that affect the IC1 region. In some people with this condition, both the maternally inherited copy and the paternally inherited copy of the IC1 region have methyl groups attached (hypermethylation). Because the IC1 region controls the genomic imprinting of the *H19* and *IGF2* genes, this abnormality disrupts the regulation of both genes. Specifically, hypermethylation of the IC1 region leads to a loss of *H19* gene activity and increased activity of the *IGF2* gene in many tissues. A loss of *H19* gene activity, which normally restrains growth, and an increase in *IGF2* gene activity, which

promotes growth, together lead to overgrowth in people with Beckwith-Wiedemann syndrome.

In a few cases, Beckwith-Wiedemann syndrome has been caused by deletions of a small amount of DNA from the IC1 region. Like abnormal methylation, these deletions alter the activity of the *H19* and *IGF2* genes.

breast cancer

Russell-Silver syndrome

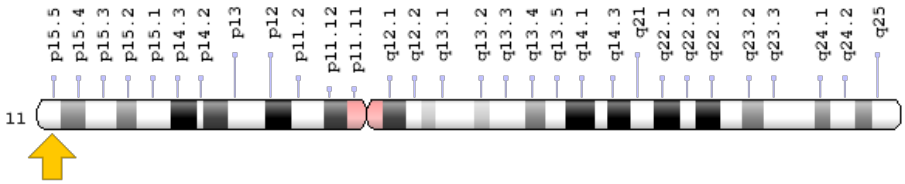
Changes in methylation of the IC1 region are also responsible for some cases of Russell-Silver syndrome, a disorder characterized by slow growth before and after birth. The changes are different than those seen in Beckwith-Wiedemann syndrome and have the opposite effect on growth.

In Russell-Silver syndrome, the paternally inherited copy of the IC1 region often has too few methyl groups attached (hypomethylation). Hypomethylation of the IC1 region leads to increased activity of the *H19* gene and a loss of *IGF2* gene activity in many tissues. An increase in *H19* gene activity, which restrains growth, and a loss of *IGF2* gene activity, which normally promotes growth, together lead to poor growth and short stature in people with Russell-Silver syndrome.

Chromosomal Location

Cytogenetic Location: 11p15.5, which is the short (p) arm of chromosome 11 at position 15.5

Molecular Location: base pairs 1,995,176 to 2,001,466 on chromosome 11 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ASM
- ASM1
- D11S813E

- H19, imprinted maternally expressed transcript
- LINC00008
- MGC4485
- PRO2605

Additional Information & Resources

Educational Resources

- The Cell: A Molecular Approach (second edition, 2000): DNA Methylation
  https://www.ncbi.nlm.nih.gov/books/NBK9904/#A1014

GeneReviews

- Beckwith-Wiedemann Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1394
- Russell-Silver Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1324

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28H19%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- H19, IMPRINTED MATERNALLY EXPRESSED NONCODING TRANSCRIPT
  http://omim.org/entry/103280
- H19/IGF2-IMPRINTING CONTROL REGION
  http://omim.org/entry/616186

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_H19.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=H19%5Bgene%5D
- HGNC Gene Family: Long non-coding RNAs
  http://www.genenames.org/cgi-bin/genefamilies/set/788

- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=4713
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/283120

Sources for This Summary

- Abu-Amero S, Monk D, Frost J, Preece M, Stanier P, Moore GE. The genetic aetiology of Silver-Russell syndrome. J Med Genet. 2008 Apr;45(4):193-9. Epub 2007 Dec 21. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18156438
- Cai X, Cullen BR. The imprinted H19 noncoding RNA is a primary microRNA precursor. RNA. 2007 Mar;13(3):313-6. Epub 2007 Jan 19.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17237358
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1800509/
- Eggermann T, Eggermann K, Schönherr N. Growth retardation versus overgrowth: Silver-Russell syndrome is genetically opposite to Beckwith-Wiedemann syndrome. Trends Genet. 2008 Apr; 24(4):195-204. doi: 10.1016/j.tig.2008.01.003. Epub 2008 Mar 7. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18329128
- Gabory A, Jammes H, Dandolo L. The H19 locus: role of an imprinted non-coding RNA in growth and development. Bioessays. 2010 Jun;32(6):473-80. doi: 10.1002/bies.200900170. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20486133
- Nativio R, Sparago A, Ito Y, Weksberg R, Riccio A, Murrell A. Disruption of genomic neighbourhood at the imprinted IGF2-H19 locus in Beckwith-Wiedemann syndrome and Silver-Russell syndrome. Hum Mol Genet. 2011 Apr 1;20(7):1363-74. doi: 10.1093/hmg/ddr018. Epub 2011 Jan 31.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21282187
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3049359/
- Sparago A, Cerrato F, Vernucci M, Ferrero GB, Silengo MC, Riccio A. Microdeletions in the human H19 DMR result in loss of IGF2 imprinting and Beckwith-Wiedemann syndrome. Nat Genet. 2004 Sep;36(9):958-60. Epub 2004 Aug 15.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15314640

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/H19

Reviewed: June 2015
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services